
# Current Management of Achalasia

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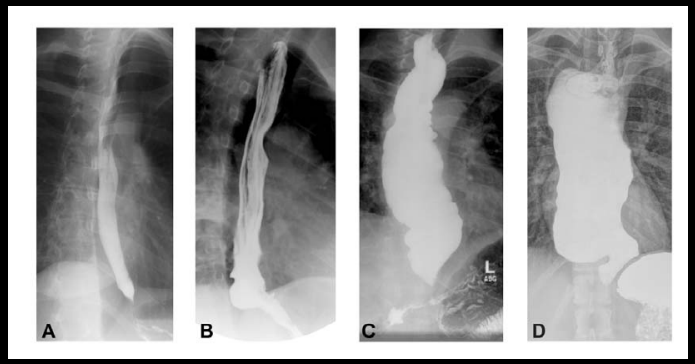
## ACHALASIA

- Definition
- Historical Perspective
- Spectrum of Disease and Patient Characteristics
- Diagnosis – Barium Swallow, EGD and Esophageal Manometry
- Options in the Management of Achalasia
  - Endoscopic Botox Injection
  - Endoscopic Dilation
  - Surgical Myotomy
- Technique for Laparoscopic Heller Myotomy, Dor Fundoplication

## ACHALASIA

- Primary Esophageal and LES Motility Disorder
  - 1764 - First treatment, whalebone padded sponge through LES.
  - Endoscopic Dilation, Botox Injection (1991)
  - Open Surgery (1913, Heller), MIS Techniques (1991)
- Incidence
  1 to 3:100.000/year (1,000 to 3,000 cases in the U.S/year)
- Clinical Picture
  Dysphagia liquids and solids – 60%
  Heartburn - 40%
- Etiology – LES primary disease (?) – Auto-Immune Mechanism (?)
  - Damage LES and Esophageal myoenteric plexus, vagal trunks and dorsal vagal nuclei.
  - Irreversible loss LES NO neurons / post-gang. PS
  - Intact post-gang. cholinergic neurons

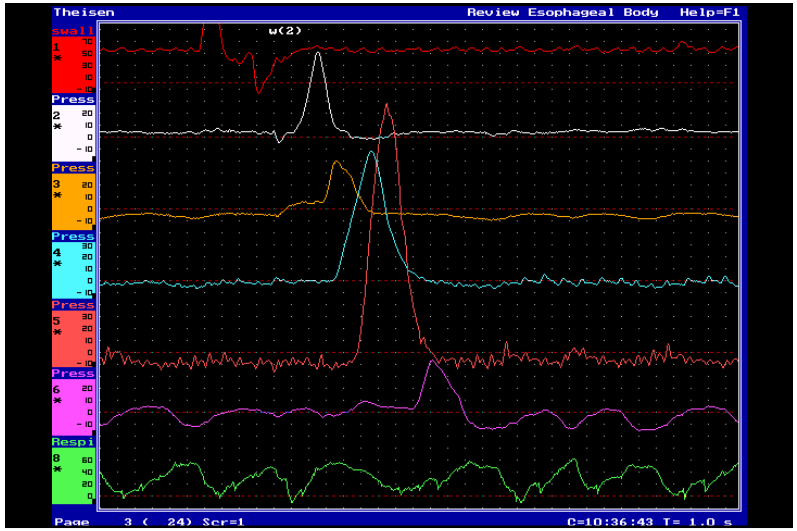
**Sugarbaker, D.J. – Primary Motor Disorders. Esophageal Surgery, New York: Churchill-Livingstone; 1995. p. 425-42.**

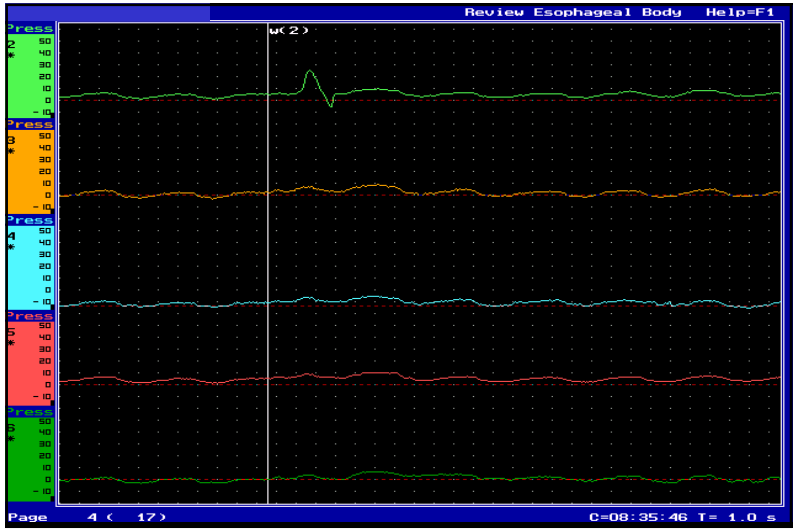



## ACHALASIA – DIAGNOSIS ESOPHAGEAL MANOMETRY

- Aperistalsis esophageal body
- Incomplete LES relaxation
- Increased LES pressure (50%)
- Elevated intra-esophageal baseline relative to gastric baseline (35%)

DeMeester, T.R.; Costantini, M. – Function Tests. Esophageal Surgery, New York: Churchill-Livingstone; 1995. p. 119-50.



## OPTIONS IN THE MANAGEMENT OF ACHALASIA

- **The goal of therapy is to promote relief of dysphagia while preventing gastroesophageal reflux (GER).**
- **Commonly used treatments are:**
  - **endoscopic botulin toxin injection (EBTI),**
  - **endoscopic balloon dilation (EBD), and**
  - **surgical myotomy with or without a fundoplication;**
- **Reported outcomes and treatment guidelines mostly come from cohort studies and expert opinions.**

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META-ANALYSIS

### Endoscopic and Surgical Treatments for Achalasia

*A Systematic Review and Meta-Analysis*

*Guilherme M. Campos, MD, PhD,* Eric Vittinghoff, PhD,† Charlotte Rabl, MD,* Mark Takata, MD,* Michael Gadenstätter, MD,‡ Feng Lin, MS,† and Ruxandra Ciovica, MD**

**Background:** Although rare, esophageal achalasia is the best described primary esophageal motility disorder. Commonly used treatments are endoscopic botulin toxin injection (EBTI), endoscopic balloon dilation (EBD), and surgical myotomy with or without a fundoplication; however, reported outcomes mostly come from cohort studies.

**Objective:** To summarize and compare the safety and efficacy of endoscopic and surgical treatments for esophageal achalasia.

**Methods:** A systematic electronic Medline literature search of articles on esophageal achalasia. Treatment options reviewed included EBTI, EBD, and surgical myotomy using open and minimally invasive techniques. Main outcome measures were frequency of symptom relief, prevalence of post-treatment gastroesophageal reflux (GER), and complications. Outcome probability was estimated using weighted averages of the sample prevalence in each study, with weights equal to the number of patients. Outcomes, within or across studies, were compared using meta-analysis and meta-regression, respectively.

**Results:** A total of 105 articles reporting on 7855 patients were selected, tabulated and reviewed. Symptom relief after EBD was better than after EBTI (68.2% vs. 40.6%; OR 3.4; 95% CI, 1.2–9.8; $P = 0.02$), and the need for additional therapy was greater for patients receiving EBTI (46.6% vs. 25%; OR, 2.6; 95% CI, 1.05–6.5. $P = 0.04$). Laparoscopic myotomy, when combined with an antireflux procedure, provided better symptom relief (90%) than all endoscopic and other surgical approaches and a low complication rate (6.3%). The incidence of postoperative GER was lower when a fundoplication was added to a laparoscopic myotomy (31.5% without a fundoplication vs. 8.8% with; OR, 6.3; 95% CI, 2.0–19.4; $P = 0.003$).

**Conclusions:** EBD is superior to EBTI. Laparoscopic myotomy with fundoplication was the most effective surgical technique and can be considered the operative procedure of choice.

(*Ann Surg* 2009;249: 45–57)

peristalsis, leading to dysphagia and other associated symptoms. It has been described from infancy through the ninth decade of life, although it occurs most commonly between the ages of 20 and 40 years. There seems to be no association with gender or race.

The goal of therapy is to promote relief of dysphagia while preventing gastroesophageal reflux (GER). This can be accomplished by reducing both the resting and swallow-induced residual pressures of the LES. Several available treatments can be tailored to the patient's overall health condition and preferences, but there is no specific therapy for managing the underlying disease process because the pathogenesis for the acquired esophageal peristalsis and LES relaxation is still unknown. None of the treatment options re-establish normal muscle activity of the esophageal body and LES. Instead, all relieve the functional obstruction caused by the failure of LES to relax upon deglutition.

The expected annual incidence of achalasia is 1 to 3 per 100,000 persons in the Western world.[7] Consequently, only a few randomized controlled trials are available, and cohort studies and expert opinions have been used to develop guidelines for treatment. Furthermore, publication bias and heterogeneity among the published articles may affect the summary estimates of systematic reviews. Nevertheless, the large number of patients studied is an advantage of large systematic reviews such as ours, and when combined with appropriate study selection and data extraction, possibly dissipates some of the limitations indicated. The aim of this article is to summarize and compare the efficacy and morbidity of endoscopic and surgical treatment options for esophageal achalasia based on the results of a systematic literature review and meta-analysis of articles on esophageal achalasia published between 1975 and 2006.

## OBJECTIVE

- **To summarize and compare the <u>efficacy and morbidity</u> of endoscopic and surgical treatment for esophageal achalasia based on the results of a systematic literature review and meta-analysis of articles on esophageal achalasia published between 1975 and 2006.**

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## METHODS

**<u>Treatments reviewed</u>**

- <u>Endoscopic botulinum toxin injection</u> **<u>(EBTI)</u>**,
- <u>Endoscopic balloon dilation</u> **<u>(EBD)</u>** using 30 to 40 mm diameter balloons, other endoscopic dilation methods **<u>(ED)</u>** used in the available randomized controlled trials,
- **<u>Surgical myotomy</u>** open transabdominal, open transthoracic, thoracoscopic or laparoscopic techniques, with/without fundoplication.

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## METHODS

- **% patients with symptom improvement:** improvement + complete relief symptoms.
- **overall posttreatment GER:** posttreatment GER symptoms + posttreatment GER using 24h pH monitoring
- **posttreatment GER 24h pH monitoring:** calculated separately.
- Complications.

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## RESULTS

- 3,478 articles identified and screened
- **105 articles - 7,855 patients selected**
- 98 articles cohort studies
  - 41 prospective cohorts/case control series
  - 57 retrospective cohorts/case control series
- 7 articles randomized controlled trials.

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## RESULTS

| | Articles | n patients |
|---|---|---|
| • Endoscopic Botox Injection | 9 | 315 |
| • Endoscopic Balloon Dilation | 15 | 1,065 |
| • EBTI vs. ED | 7 | 261 |
| • ED vs. surgical myotomy | 10 | 1,373 |
| • Open transabdom. myotomy | 10 | 732 |
| • Transthoracic myotomy | 13 | 842 |
| • Thoracoscopic myotomy | 8 | 211 |
| • Laparoscopic myotomy | 39 | 3,086 |

Six articles reported results for two myotomy techniques.

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TABLE 5. Results Obtained With Open Transabdominal Myotomy in the Treatment of Achalasia

| Author | Year | Design | N All | Follow-up (mo) | N With ARP | N Without ARP | Symptom Improvement: All N (%) | Symptom Improvement: With ARP N (%) | Symptom Improvement: Without ARP N (%) | Evidence of GER: All n/N* (%) | Evidence of GER: With ARP n/N* (%) | Evidence of GER: Without ARP n/N* (%) | Complications N (%) | Mortality N (%) |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Bloch[69] | 1976 | RC | 108 | 48 | 11 | 97 | 71 (66) | 11 (100) | 64 (66) | 20/108 (19) | 0/11 (0) | 20/97 (21) | 4 (4) | 0 (0) |
| Veiga-Fernandes[81] | 1981 | RC | 15 | 22 | 15 | — | 15 (100) | 15 (100) | — | 0/15 (0) | 0/15 (0) | — | — | 0 (0) |
| Jaakkola[82] | 1991 | RC | 26 | 104 | 4 | 22 | 12 (46) | — | — | 9/23 (39) | 0/4 (0) | 14/22 (64) | 16 (62) | 0 (0) |
| Bonavina[83] | 1992 | RC | 206 | 66 | 206 | — | 194 (94) | 194 (94) | — | 7/81 (9)† | 7/81 (9) | — | 2 (1) | 0 (0) |
| Picciocchi[68] | 1993 | RC | 101 | 114 | 80 | 21 | 90 (89) | 72 (90) | 12 (57) | 8/74 (11)† | 4/58 (7) | 4/16 (25) | 6 (6) | 0 (0) |
| Arcomi[85] | 1995 | RC | 17 | 8 | 17 | — | 17 (100) | 17 (100) | — | 1/17 (6)† | 1/17 (6) | — | 0 (0) | 0 (0) |
| Douard[86] | 2004 | PC | 30 | 51 | 30 | — | 28 (93) | 28 (93) | — | 2/30 (7) | 2/30 (7) | — | 17 (57) | 0 (0) |
| Mineo[87] | 2004 | PC | 39 | 107 | 39 | — | 35 (90) | 35 (90) | — | 3/39 (8)† | 3/39 (8) | — | 0 (0) | 0 (0) |
| Csendes[88] | 2006 | PC | 67 | 190 | 67 | — | 49 (73) | 49 (73) | — | 2/13 (15)† | 2/13 (15) | — | 2 (3) | 0 (0) |
| Mattioli[89] | 2006 | PC | 123 | 105 | 123 | — | 108 (88) | 108 (88) | — | 10/123 (8) | 10/123 (8) | — | — | — |
| | | | | | | | | Mean (Range) | | | | | | |
| Total | | | 732 | 87.4 (8–190) | 592 | 140 | 84.5 (48–100) | 89.7 (73–100) | 64.4 (57–66) | 12 (0–39) | 7.5 (0–15) | 28.5 (2–64) | 4.7 (6.4) | 0 (0) |

*n indicates number of patients with GER; N, number of patients evaluated for GER.
†Cohorts where gastroesophageal reflux was evaluated by 24-hour pH monitoring.
PC indicates prospective cohort/case control series; RC, retrospective cohort/case control series; ARP, antireflux procedure; GER, gastroesophageal reflux.

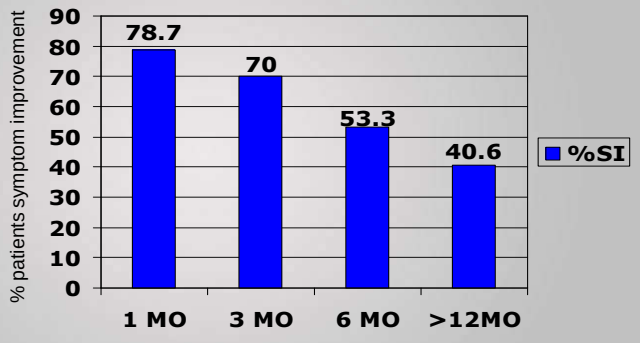
TABLE 6. Results Obtained With Open Transthoracic Myotomy in the Treatment of Achalasia

| Author | Year | Design | N All | Follow-up (mo) | N With ARP | N Without ARP | Symptom Improvement: All N (%) | Symptom Improvement: With ARP N (%) | Symptom Improvement: Without ARP N (%) | Evidence of GER: All n/N* (%) | Evidence of GER: With ARP n/N* (%) | Evidence of GER: Without ARP n/N* (%) | Complications N (%) | Mortality N (%) |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Manson[90] | 1976 | RC | 34 | 120 | 9 | 25 | 32 (94) | 9 (100) | 24 (94) | 9/34 (26) | 0/9 (0) | 9/25 (36) | — | 0 (0) |
| Jara[91] | 1979 | RC | 145 | 85 | — | 121 | 116 (80) | — | 97 (80) | 58/121 (48) | — | 58/121 (48) | — | 0 (0) |
| Pai[92] | 1984 | RC | 35 | 65 | 20 | 15 | 30 (86) | 16 (80) | 14 (93) | 3/33 (9) | 2/17 (12) | 1/16 (6) | 3 (9) | 1 (3) |
| Goulbourne[93] | 1985 | RC | 65 | 100 | — | 65 | 52 (80) | — | 52 (80) | — | — | — | — | 0 (0) |
| Stipa[94] | 1990 | RC | 101 | 80 | 101 | — | 78 (77) | 79 (78) | — | 11/96 (11) | 11/92 (12) | — | 4 (4) | 0 (0) |
| Jaakkola[82] | 1991 | RC | 34 | 172 | — | 34 | 33 (97) | — | 33 (97) | 1/23 (4) | — | 1/23 (4) | 5 (15) | 0 (0) |
| Ellis[95] | 1993 | RC | 179 | 108 | — | 179 | 159 (89) | — | 159 (89) | 9/179 (5) | — | 9/179 (5) | 16 (9) | 0 (0) |
| Mathisen[96] | 1994 | RC | 22 | 168 | 22 | — | 15 (68) | 15 (68) | — | 4/22 (18) | 4/22 (18) | — | — | — |
| Ferguson[97] | 1996 | RC | 60 | 57 | 60 | — | 53 (88) | 53 (88) | — | 6/51 (12) | 6/51 (12) | — | 3 (5) | 0 (0) |
| Shaf[98] | 1999 | RC | 47 | 88 | — | 47 | 44 (94) | — | 44 (94) | 31/47 (66) | — | 31/47 (66) | — | 0 (0) |
| Jonas[99] | 2001 | RC | 16 | 102 | — | 16 | 14 (88) | — | 14 (88) | — | — | — | 0 (0) | 0 (0) |
| Lindenmann[100] | 2005 | RC | 40 | 120 | — | 40 | 34 (85) | — | 34 (85) | 18/40 (45)† | — | 18/40 (45) | — | — |
| Gaissert[54] | 2006 | RC | 64 | 154 | 15 | 49 | 41 (64) | 10 (67) | 32 (65) | 20/52 (38) | 4/14 (29) | 16/38 (42) | 8 (13) | 0 (0) |
| | | | | | | | | Mean (Range) | | | | | | |
| Total | | | 842 | 102 (57–172) | 227 | 591 | 83.3 (64–97) | 80.2 (64–100) | 85.1 (66–97) | 24.6 (4–66) | 13.6 (0–28) | 29.2 (4–66) | 39 (4.6) | 1 (0.1) |

*n indicates number of patients with GER; N, number of patients evaluated for GER.
†Cohorts where gastroesophageal reflux was evaluated by 24-hour pH monitoring.
RC indicates retrospective cohort/case control series; ARP, antireflux procedure; GER, gastroesophageal reflux.

## Endoscopic Botox Injection
## 9 articles (315 patients)

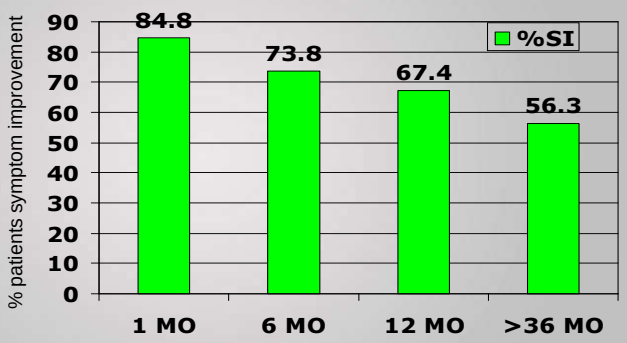
Mean follow-up: 18 mo (6-30mo)




153 patients (48.5%) needed repeated treatment

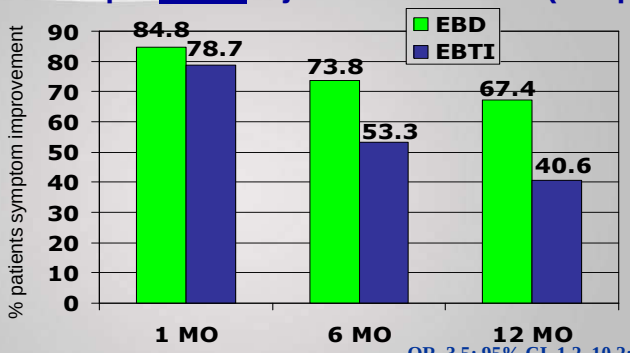
## Endoscopic Balloon Dilation
## 15 articles (1,065 patients)

Mean follow-up: 31 mo (6-111mo)




279 patients (26.2%) needed repeated treatment, 17 (1.6%) perforation

## Endoscopic Balloon Dilation: 15 articles (1,065 pts.)
## Endoscopic Botox Injection: 9 articles (315 pts.)




OR, 3.5; 95% CI, 1.2–10.2; P=0.03

EBTI: 153 pts. (48.5%) repeated treatment

EBD: 279 pts. (26.2%) repeated treatment, 17 (1.6%) perforation

## Meta-regression analyses of outcomes after EBTI or EBD

**Better SI at 12 months when EBD was used (67.4% vs. 40.6%; OR 3.5, 95% CI 1.2 to 10.2, p=0.03).**

**The need additional therapy greater receiving EBTI (48.5% vs. 26.2%; OR 2.7, 95% CI 1.04 to 7.1, p=0.04).**

### 7 RCT's and Prospective cohorts EBTI vs. ED (261 pts)

**Greater decrease LES pressure, ED vs. EBTI**

52% vs. 30%, p=0.07

**Greater % pts. with SI, ED vs. EBTI**

68% vs. 24%; OR 6.4, 95% CI 3.4 to 12.0, p<0.01

**Perforation rate ED higher than EBD only**

11.2% vs. 1.6%; OR 17.6, 95% CI 3.9 to 80.9, p=0.002

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# RESULTS

- **EBTI:** 9 articles (315 patients)
- **EBD:** 15 articles (1,065 patients)
- **EBTI vs. ED:** 7 articles (261 patients)
- **ED vs. surgical myotomy:** 10 articles (1,373 patients)
- **Open transabdominal myotomy:** 10 articles (732 patients)
- **Transthoracic myotomy:** 13 articles (842 patients)
- **Thoracoscopic myotomy:** 8 articles (211 patients)
- **Laparoscopic myotomy:** 39 articles (3,086 patients)

Six articles reported results for two myotomy techniques.

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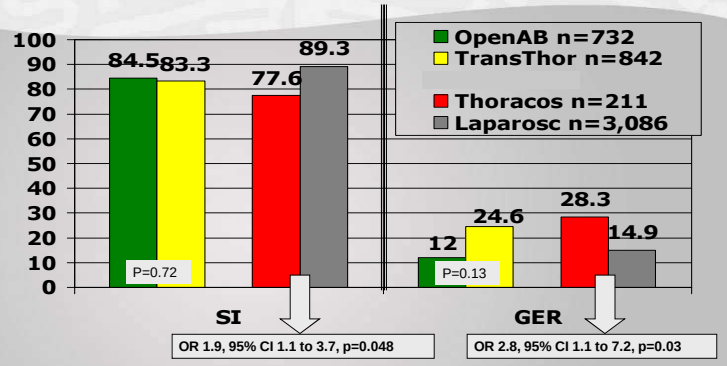
## Results - Open and MIS Myotomy

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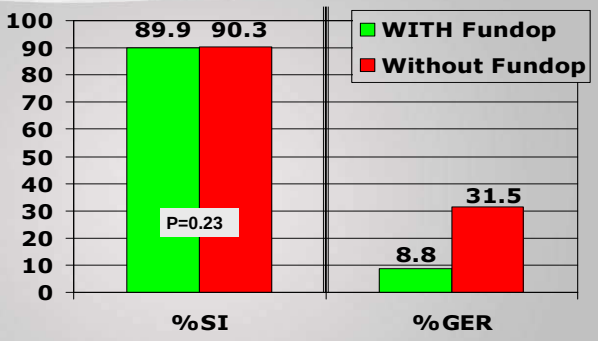
## SI and GER after Laparoscopic Myotomy (n=3,086) With (n=2,526) and Without (n=560) ARP




OR 4.3, 95% CI 1.9 to 9.7, p=0.0001

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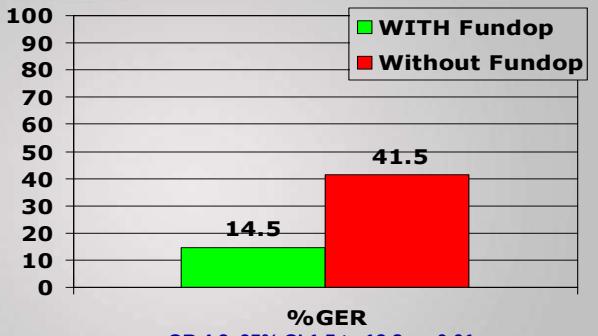
## Abnormal 24 pH after Laparoscopic Myotomy, n=725 With (n=583) and Without (n=142) ARP




OR 4.2, 95% CI 1.5 to 12.8, p=0.01

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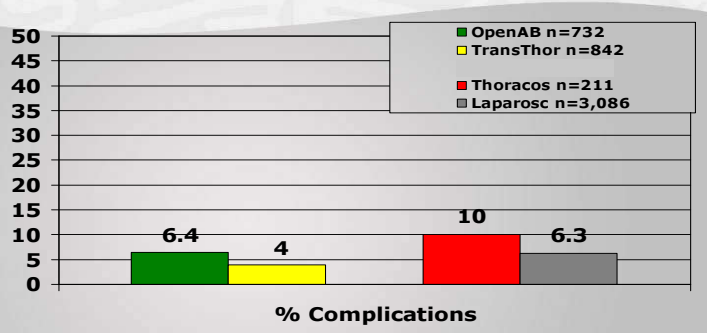
## Results - Open and MIS Myotomy

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## Analyses of outcomes after Surgical Myotomy vs. Dilation

**Intra-operative perforation lap. Myotomy:** 182 patients (6.9%).
All inadvertent injuries repaired during the index operation.
*** 19 (0.7%) pts. developed post-operative manifestations**

Perforation EBD similar laparoscopic myotomy
(1.6% vs. 0.7%; OR 1.7, 95%C.I. 0.8 to 3.7; p=0.14)

Perforation ED higher laparoscopic myotomy
(8.8.% vs. 0.7%; OR 13.3, 95%C.I. 7.8 to 22.8; p<0.01).

Complications laparoscopic myotomy was higher than for EBD only
(6.3% vs. 1.6%; OR 3.0, 95%C.I. 1.5 to 6.3; p=0.004)
Similar to ED
(6.3% vs. 8.8%; OR 0.8, 95%C.I. 0.6 to 1.1; p=0.2).

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## LIMITATIONS

- Rare nature of achalasia and few controlled trials available.
- Heterogeneity and publication bias may impact the results.
- Control for heterogeneity by defining *a priori:* inclusion and exclusion criteria and the outcomes to be studied
- When compared pooled data of all cohorts to controlled trials, results and conclusions were concordant.
- Large number of patients studied is an advantage of large systematic reviews, and possibly dissipates some of the limitations indicated.

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## CONCLUSIONS

- EBD is superior to EBTI.
- Laparoscopic myotomy with fundoplication was the most effective surgical technique and can be considered the procedure of choice and first line of treatment for most patients.

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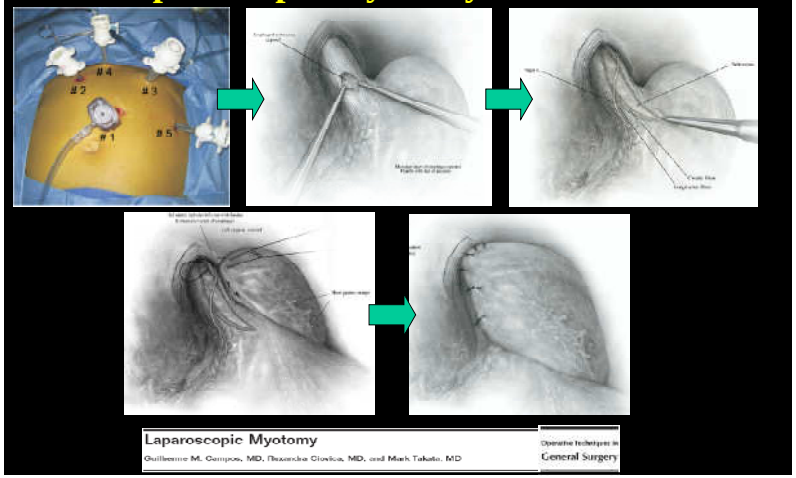
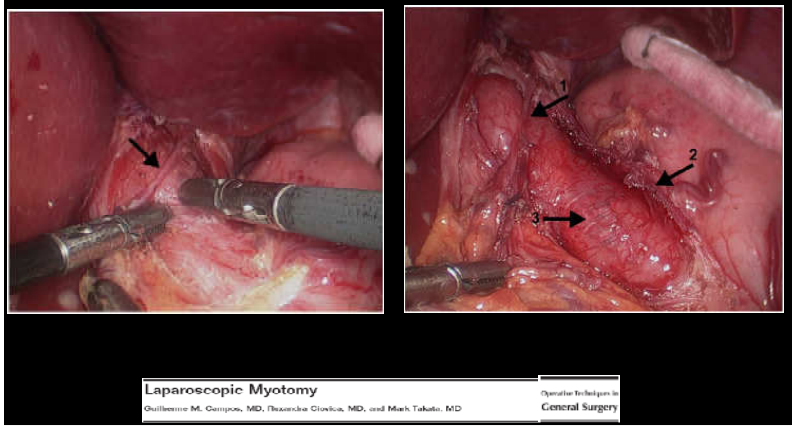
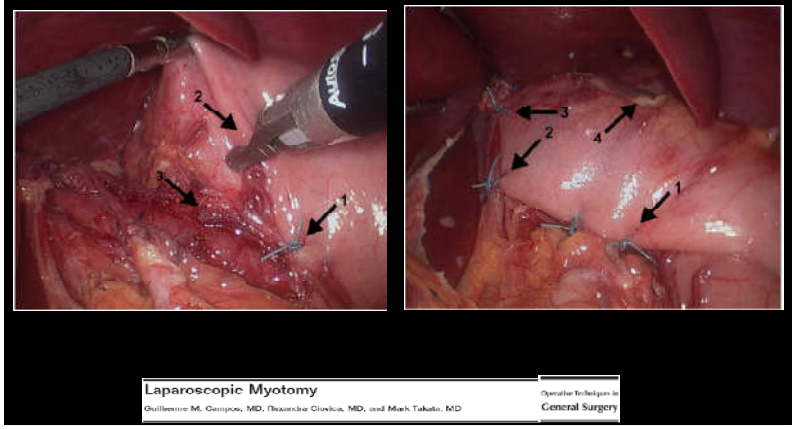
## Laparoscopic Myotomy for Achalasia




## Laparoscopic Heller Myotomy for Achalasia




## Laparoscopic Heller Myotomy for Achalasia



## CONCLUSIONS

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- **Laparoscopic myotomy with fundoplication was the most effective surgical technique and can be considered the procedure of choice and first line of treatment for most patients.**

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